

Congenital Heart Disease

Diagnosis of Pulmonary Hypertension in the Congenital Heart Disease Adult Population

Impact on Outcomes

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Objectives	The aim of this study was to assess the impact of the diagnosis of pulmonary hypertension (PH) on mortality, morbidity, and health services utilization (HSU) in an adult congenital heart disease (CHD) population.
Background	Although PH is a well-recognized complication of CHD, population-based studies of its significance on the survival and functional capacity of patients are uncommon.
Methods	A retrospective longitudinal cohort study was conducted in an adult CHD population with 23 years of follow-up, from 1983 to 2005. The prevalence of PH was measured in 2005. Mortality, morbidity, and HSU outcomes were compared between patients with and without diagnoses of PH using multivariate Cox (mortality and morbidity) and Poisson (HSU) regression models within a subcohort matched for age and CHD lesion type.
Results	Of 38,430 adults alive with CHD in 2005, 2,212 (5.8%) had diagnoses of PH (median age 67 years, 59% women). The diagnosis of PH increased the all-cause mortality rate of adults with CHD more than 2-fold compared with patients without PH (hazard ratio [HR]: 2.69; 95% confidence interval [CI]: 2.41 to 2.99). Morbid complications including heart failure and arrhythmia occurred with a 3-fold higher risk compared with patients without PH (HR: 3.01; 95% CI: 2.80 to 3.22). The utilization of inpatient and outpatient services was increased, especially cardiac catheterization, excluding the index diagnostic study (rate ratio: 5.04; 95% CI: 4.27 to 5.93) and coronary and intensive care hospitalizations (rate ratio: 5.03; 95% CI: 4.86 to 5.20).
Conclusions	A diagnosis of PH in adults with CHD is associated with a more than 2-fold higher risk for all-cause mortality and 3-fold higher rates of HSU, reflecting high morbidity. (J Am Coll Cardiol 2011;58:538–46) © 2011 by the American College of Cardiology Foundation

Advances in both medical and surgical care have resulted in an increasing prevalence of adults with congenital heart disease (CHD) (1). Even without severe cardiac lesions, these adults have high rates of health care resource utilization (2). Pulmonary hypertension (PH) is a well-recognized complication limiting the survival and functional capacity of patients with surgically unrepaired, palliated, and in some cases “repaired” CHD (3–9). The past few decades have

witnessed earlier detection and intervention for CHD, but the morbidity and mortality of patients with CHD-related PH remains unknown. Studies of CHD-related PH have been published from tertiary hospital registry data, with emphasis on Eisenmenger syndrome and pediatric study populations (7,10). We sought to assess the impact of the diagnosis of PH in an adult CHD population by describing the prevalence of PH and its incremental effect on mortality, morbidity, and health services utilization (HSU).

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Methods

Data sources. In Quebec, Canada, universal access to health care is provided, and a unique health care number assigned at birth is systematically linked to all diagnoses, hospitalizations, and health services rendered. The database of Régie de l'Assurance Maladie du Québec (RAMQ) records physicians' services claims, and the Med-Echo database records information related to inpatient care.

A population-based database comprising 71,467 patients with CHD followed for >1.5 million patient-years was constructed by merging the 2 administrative provincial databases (1). Diagnostic codes adhered to the International Classification of Diseases–Ninth Revision (ICD-9). Patients were identified if they had at least 1 diagnostic code for CHD and/or CHD-specific surgical procedure (Online Appendix) made only by cardiologists, primary care physicians, and cardiovascular surgeons and were assigned CHD diagnoses using a previously defined hierarchical algorithm (1). By law, attestation of death is sent to the Quebec Health Insurance Board, making documentation of death complete with the exception of rare fraudulent omissions. The database therefore contained comprehensive longitudinal, diagnostic, and therapeutic records of all patient-linked health care encounters from January 1983 to December 2005 for all Quebec residents with CHD.

The McGill University Health Centre Ethics Board and the Quebec government agency responsible for privacy of access to information approved the study.

Study population. For the purposes of this study, we derived 2 retrospective cohorts from Quebec's CHD database (Fig. 1) that included patients age ≥ 18 years. The study population for the prevalence objective included all adults with CHD alive in 2005, irrespective of a PH diagnosis in the database over the past 23 years. The matched cohort included adults with their first PH diagnosis coding in the database between 1990 and 2005 and controls of the same age and CHD lesion type but without diagnoses of PH up until the time when the diagnosis was made for the cases. Thus, time zero for each matched PH and non-PH pair was the time of the first PH diagnosis of the case. When multiple controls were available for matching, 1 was randomly chosen. One-to-one matching was sought for the 3,005 patients age ≥ 18 years, but matches could not be identified for 233 patients. The final number of patients in the matched cohort (Fig. 1) was 5,544 (2,772 matched 1:1). The matched cohort excluded subjects with PH diagnoses from 1983 to 1990 (the washout period) to increase the yield of newly diagnosed PH cases.

CHD lesions were grouped as either severe CHD, shunts, valvular, or other (Table 1, column 1). Severe CHD lesions reflected patients with a high likelihood of cyanosis or requiring surgery early in life.

Study design. The PH period prevalence was estimated in 2005 as the proportion of patients in the prevalence cohort that received initial PH diagnoses between January 1983 and December 2005. The effect of a PH diagnosis on the mortality, morbidity, and HSU of patients with CHD was estimated with a retrospective matched cohort, whereby patients with diagnoses of PH were matched for age, CHD lesion type and time to non-PH patients. Subjects in the matched cohort were followed for a maximum of 15 years, until they experienced an outcome of interest or to the end of the study, whichever occurred first. Once selected as a

control, a subject was kept in all analyses, regardless of whether he or she subsequently developed PH.

Measurements. PH MEASUREMENT. Patients with PH were included if a diagnosis of primary or secondary PH (Online Appendix) was made by selected specialists (cardiologists, pulmonologists, pediatricians, cardiothoracic surgeons, anesthesiologists, and emergency and general physicians) in the RAMQ or Med-Echo databases.

OUTCOMES MEASUREMENT (MATCHED COHORT). Death during follow-up in the matched cohort defined mortality. Morbid complications assessed are presented in the Online Appendix with identifying ICD-9 codes.

HSU was measured in the first 5 years of follow-up using database-specific codes for physician specialty, medical procedure, and institution type, including outpatient consultations with cardiologists, pulmonologists, cardiothoracic surgeons, neurosurgeons, anesthesiologists, hematologists, neurologists, obstetricians, pediatricians, radiologists, nephrologists, geriatricians, and general, family, and emergency physicians; hospitalization days; emergency department visits and intensive and coronary care unit admissions; and echocardiography and cardiac catheterization (excluding the index diagnostic catheterization or echocardiographic study performed within 1 year of the first PH diagnosis coding).

CONFOUNDERS MEASUREMENT (MATCHED COHORT). Confounders included age, sex, CHD lesion, clinical diagnoses known to be risk factors for PH and mortality, and the overall burden of disease measured by the Charlson index (11). Age and CHD lesion type groups (Table 1) were controlled for by matching. Sex, confounding clinical diagnoses, and the overall burden of disease were controlled for by statistical adjustment.

Confounding medical diagnoses were identified using ICD-9 codes (Online Appendix) and measured for each PH case–non-PH control pair within the 5 years before the time when the PH case was diagnosed, with the exception of human immunodeficiency virus infection (10 years before). Higher index scores have been associated with increased morbidity and mortality (12).

Statistical analysis. Descriptive statistics include medians, interquartile ranges, and proportions. The prevalence of PH was defined as the ratio between the number of adult patients with CHD alive in 2005 who had PH diagnoses from 1983 to 2005 and the total adult CHD population alive in 2005.

Abbreviations and Acronyms

ASD = atrial septal defect

CHD = congenital heart disease

CI = confidence interval

HR = hazard ratio estimated from Cox proportional hazards regression

HSU = health services utilization

ICD-9 = International Classification of Diseases–Ninth Revision

PH = pulmonary hypertension

RR = rate ratio estimated from Poisson regression

VSD = ventricular septal defect

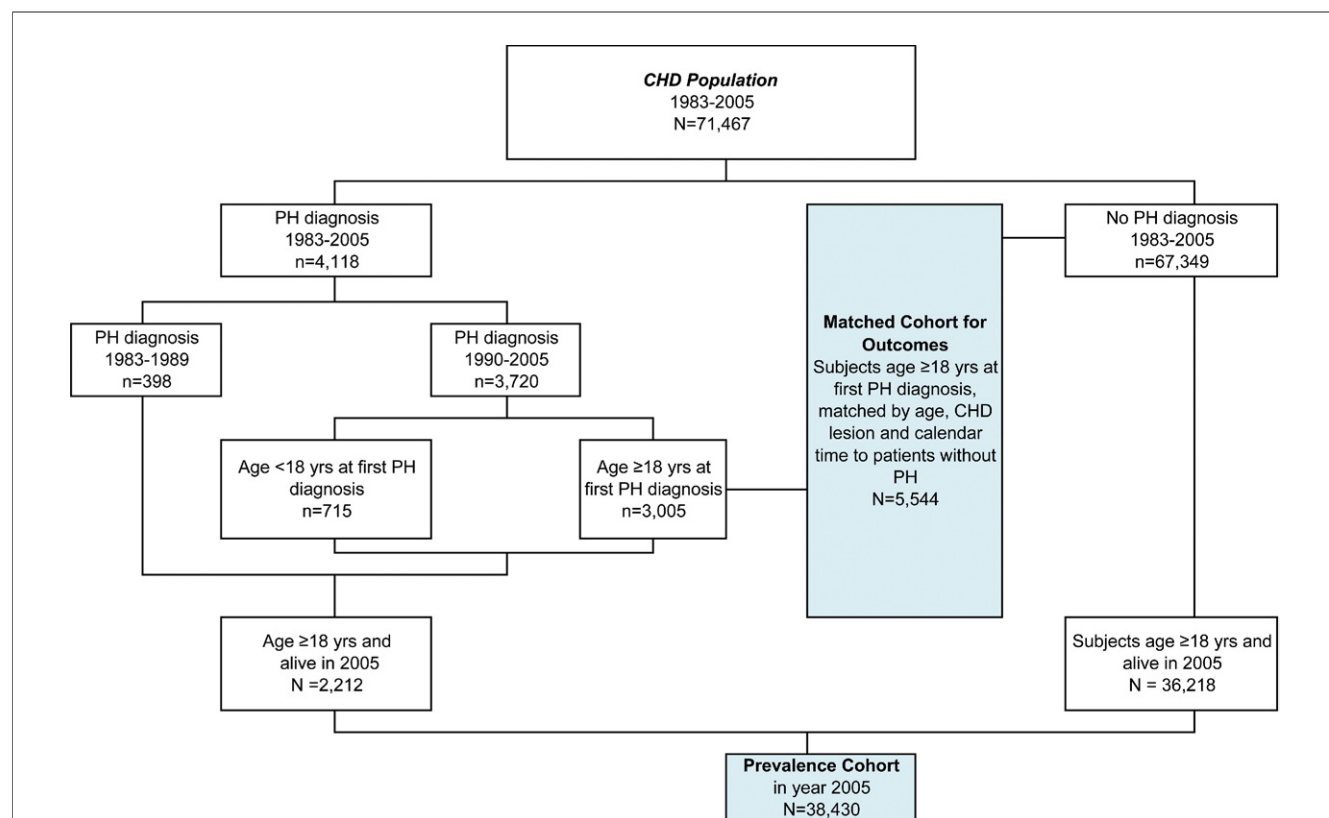


Figure 1 Study Population and Design

The figure illustrates the derivation of the study population for the prevalence and matched cohorts. CHD = congenital heart disease; PH = pulmonary hypertension.

The effect of PH diagnosis on mortality in different age groups was analyzed using Kaplan-Meier plots stratified by age groups (18 to 39 years, 40 to 64 years, and ≥ 65 years) in the matched cohort.

Regression analyses adjusted for confounding variables estimated the effect of PH diagnosis on morbidity and mortality (Cox regression) and HSU (Poisson regression) outcomes. The regression analyses were not adjusted for matching, because no imbalance was expected between the exposed and unexposed study subjects with respect to loss to follow-up and/or missing data in administrative databases (13). The morbidity outcome was defined as the time to the first of any of the 9 PH morbid outcome conditions (Online Appendix). All confounders were chosen on the basis of a priori knowledge and retained in the model regardless of their statistical significance. The proportionality of hazards assumption was assessed using the plot of the log(-log (estimated survival distribution function)) versus log (time), with no violation detected. From the Poisson analysis, we report rate ratios (RRs) and 95% confidence intervals (CIs), while from the Cox analysis we report hazard ratios (HRs) and 95% CIs. All statistical analyses were performed using SAS version 9.1 (SAS Institute Inc., Cary, North Carolina). **Sensitivity analyses.** To maximize the identification of PH cases, the main analyses included all PH diagnoses made by

selected specialists, irrespective of whether a diagnostic test for PH was performed at the time of the first PH coding in the database (some diagnoses are carried over from visits occurring before the start of the database). Acknowledging that cardiac catheterization is the clinical reference standard to diagnose PH, we performed a sensitivity analysis restricted to PH and non-PH pairs for which the PH case had a cardiac catheterization within ± 1 year of the first PH diagnosis.

Results

PH prevalence. The clinical characteristics of the prevalence cohort are presented in Table 1. Of 38,430 adults alive with CHD in 2005, 2,212 had diagnoses of PH (prevalence 58 in 1,000). Patients with CHD-related PH were older (difference in median age 26 years), and there were proportionately more women in the CHD population with PH compared with those without PH. Shunts were the most common type of CHD lesion among patients with PH.

PH outcomes. When PH complicated adults with CHD, the risks for all outcomes assessed were increased compared with patients without PH (Figs. 2 and 3).

All-cause mortality risk was more than 2-fold higher for patients with PH diagnoses compared with those without

Table 1 Clinical Characteristics of the Prevalence Cohort

Variable	Adults With CHD (n = 38,430)	CHD With PH (n = 2,212)	CHD Without PH (n = 36,218)	p Value
Age (yrs)	42 (28–63)	67 (51–77)	41 (27–61)	<0.001
Shunts CHD	35 (24–51)	63 (45–76)	34 (24–49)	<0.001
Severe CHD	33 (25–44)	39 (28–55)	33 (24–44)	<0.001
Valvular CHD	44 (27–65)	67 (55–76)	43 (27–63)	<0.001
Other CHD	56 (37–72)	73 (62–80)	54 (36–71)	<0.001
Women	21,614 (56%)	1,313 (59%)	20,301 (56%)	0.002
Death	623 (2%)	142 (6%)	481 (1%)	<0.001
CHD lesion classification				
Shunts	15,724 (41%)	837 (38%)	14,887 (41%)	<0.001
ASD	7,122 (19%)	571 (26%)	6,551 (18%)	<0.001
VSD	6,651 (17%)	153 (7%)	6,498 (18%)	<0.001
Atrioventricular canal defect	1,321 (3%)	86 (4%)	1,235 (3%)	0.230
Patent ductus arteriosus	630 (2%)	27 (1%)	603 (2%)	0.110
Severe	2,259 (6%)	149 (7%)	2,110 (6%)	0.093
Tetralogy of Fallot	1,191 (3%)	70 (3%)	1,121 (3%)	0.850
Truncus arteriosus	193 (1%)	15 (1%)	178 (1%)	0.230
Transposition of the great arteries	438 (1%)	26 (1%)	412 (1%)	0.870
Univentricular heart	326 (1%)	30 (1%)	296 (1%)	0.007
Ebstein's anomaly	111 (<1%)	8 (<1%)	103 (<1%)	0.510
Valvular	5,374 (14%)	373 (17%)	5,001 (14%)	<0.001
Congenital aortic stenosis	1,380 (4%)	82 (4%)	1,298 (4%)	<0.001
Congenital mitral regurgitation	1,389 (4%)	176 (8%)	1,213 (3%)	<0.001
Pulmonary valve anomalies	1,270 (3%)	24 (1%)	1,246 (3%)	<0.001
Other valvular	1,332 (3%)	91 (4%)	1,244 (3%)	<0.001
Other	15,073 (39%)	853 (39%)	14,220 (39%)	0.8369
Coarctation of the aorta	765 (2%)	20 (1%)	745 (2%)	<0.001
Unspecified	14,308 (37%)	833 (40%)	13,475 (37%)	0.670

Values are median (IQR) or n (%). Clinical characteristics in 2005 of adults in the prevalence cohort with and without PH and CHD. The table depicts the distribution of different cardiac congenital lesions among subjects with and without PH. Prevalence of PH in year 2005 among subjects with different cardiac congenital lesions can be estimated by dividing the number of patients with PH and a given lesion (column 3) by the number of adults with that lesion (column 2).

ASD = atrial septal defect; CHD = congenital heart disease; IQR = interquartile range; PH = pulmonary hypertension; VSD = ventricular septal defect.

(adjusted HR: 2.69; 95% CI: 2.41 to 2.99; $p < 0.001$). Kaplan-Meier plots of the matched cohort showed the greatest impact of a diagnosis of PH on the younger age group relative to their counterparts without PH (Fig. 4). Furthermore, there was an impact on mortality within the first few years after a PH diagnosis in all age groups, as indicated by early plot divergence.

The risk for morbidity was 3-fold higher in patients with CHD with PH compared with those without (HR: 3.08; 95% CI: 2.87 to 3.30; $p < 0.001$). Heart failure and arrhythmia were the most frequent complications, occurring at least once in 31% and 28% of patients with CHD-related PH during follow-up, respectively (data not shown).

Inpatient and outpatient clinical visits for any reason were increased in patients with PH (Fig. 3). Hospitalization days were increased more than 3-fold compared with those without PH (RR: 3.40; 95% CI: 3.36 to 3.44; $p < 0.0001$), especially to coronary or intensive care facilities (RR: 5.03; 95% CI: 4.86 to 5.20; $p < 0.0001$). Rates of cardiac catheterization (HR: 5.04; 95% CI: 4.27 to 5.93; $p < 0.0001$) and echocardiography (HR: 3.08; 95% CI: 2.96 to

3.21; $p < 0.0001$) after the index diagnosis of PH were significantly higher compared with patients without PH.

Sensitivity analyses. With the matched cohort study population restricted to patients who underwent cardiac catheterization within 1 year of the index PH diagnosis ($n = 861$), the impact of PH on outcomes was either similar (mortality HR: 2.34; 95% CI: 1.92 to 2.85; morbidity HR: 3.09; 95% CI: 2.72 to 3.52; hospitalization RR: 3.89; 95% CI: 3.81 to 3.98; outpatient visits RR: 1.45; 95% CI: 1.43 to 1.47; emergency department visits RR: 1.79; 95% CI: 1.72 to 1.88; echocardiography RR: 3.76; 95% CI: 3.52 to 4.03) or stronger (days in coronary or intensive care units RR: 6.41; 95% CI: 6.04 to 6.80) than the main analyses. Thus, results from the main analyses were either not affected by the inclusive noninvasive definition of PH or biased toward the null.

Discussion

In this large population-based study, we have described for the first time the significant adverse effect of a PH diagnosis

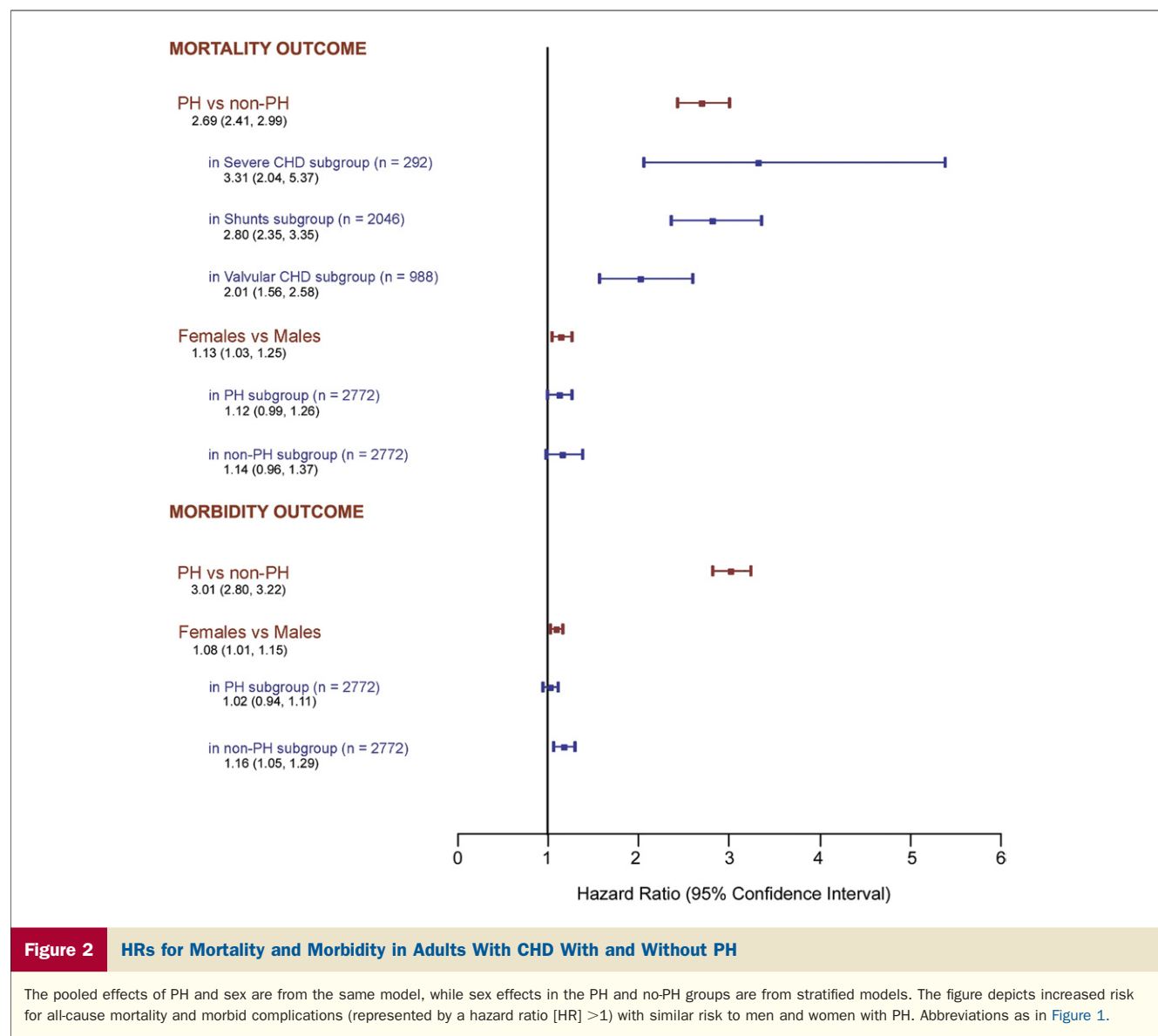


Figure 2 HRs for Mortality and Morbidity in Adults With CHD With and Without PH

The pooled effects of PH and sex are from the same model, while sex effects in the PH and no-PH groups are from stratified models. The figure depicts increased risk for all-cause mortality and morbid complications (represented by a hazard ratio [HR] >1) with similar risk to men and women with PH. Abbreviations as in Figure 1.

on survival and morbidity in adult patients with a broad range of CHD defects. PH afflicted 6% of adults alive with CHD. Although the median age of these adults was in the sixth decade of life, PH was associated with a more than doubling of all-cause mortality and tripling of morbid complications that were reflected by a more than 3-fold increase in hospitalization days, especially to coronary and intensive care units.

Prevalence. The prevalence of CHD-related PH has been reported with a wide range (6–9), dependent on the entry diagnostic criteria and populations studied.

Estimates of the prevalence of PH among the general adult CHD population have been extrapolated from tertiary hospital registries of patients with the entire spectrum of pulmonary arterial hypertension. The prevalence of patients with CHD-related PH ranges between 1.7 and 12.8 cases per million adults from these registries in Western countries

(14,15). In contrast to these studies, our source population was adults with CHD.

The risk for developing CHD-related PH is influenced by multiple factors, including increased pulmonary blood flow, pressure, the timing and success of surgical correction, extracardiac abnormalities, and genetic factors. Eisenmenger syndrome is the most advanced expression of CHD-related PH, and advances in treatments have halved the prevalence of Eisenmenger syndrome in the Western world over the past 50 years (16). The prevalence of CHD-related PH has been reported mostly in patients with septal defects and ranged from 6% to 28% (6,10,17). However, in all these studies, patients attending specialized tertiary referral hospitals and those with Eisenmenger syndrome were overrepresented.

Because provincial databases capture medical visits beyond the tertiary hospital setting, our reported prevalence is

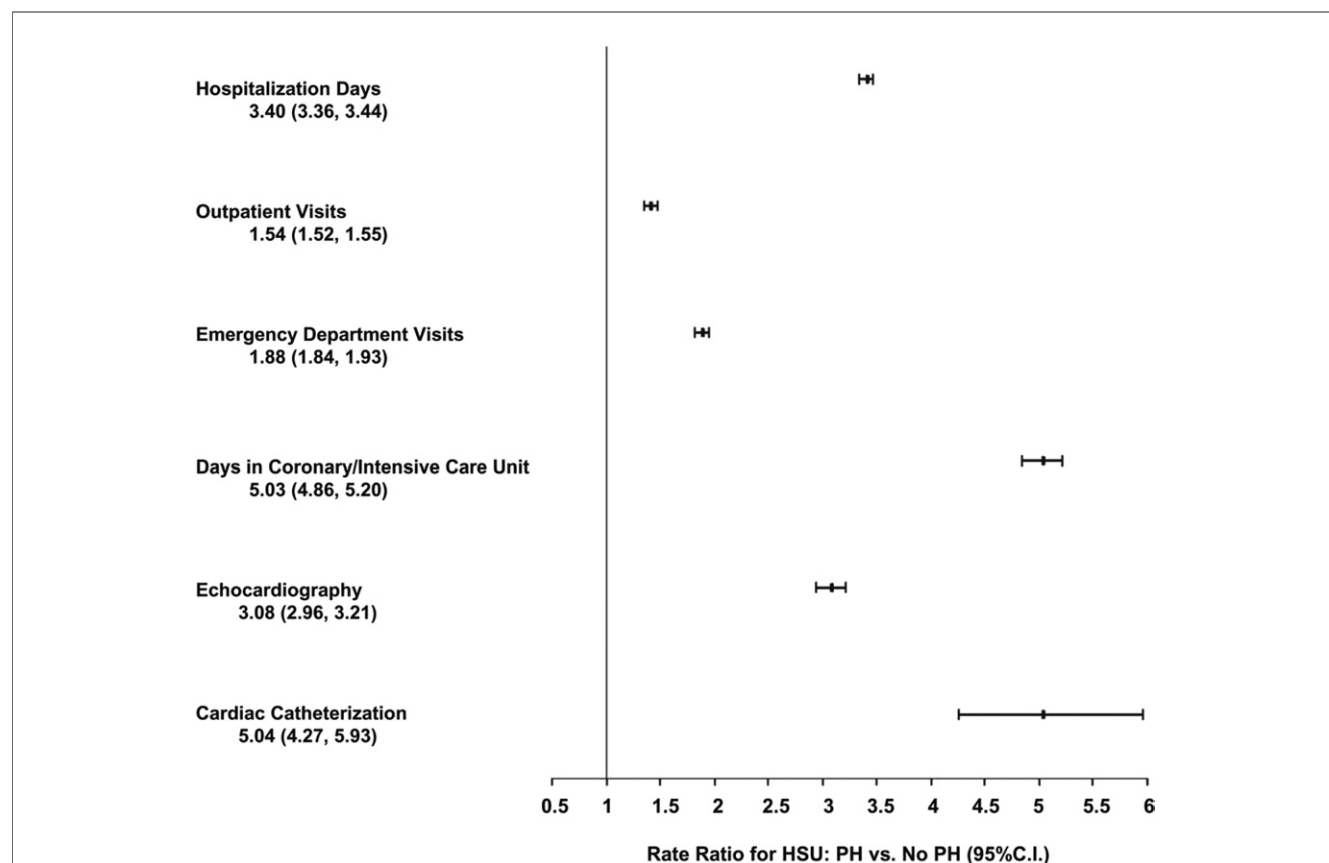


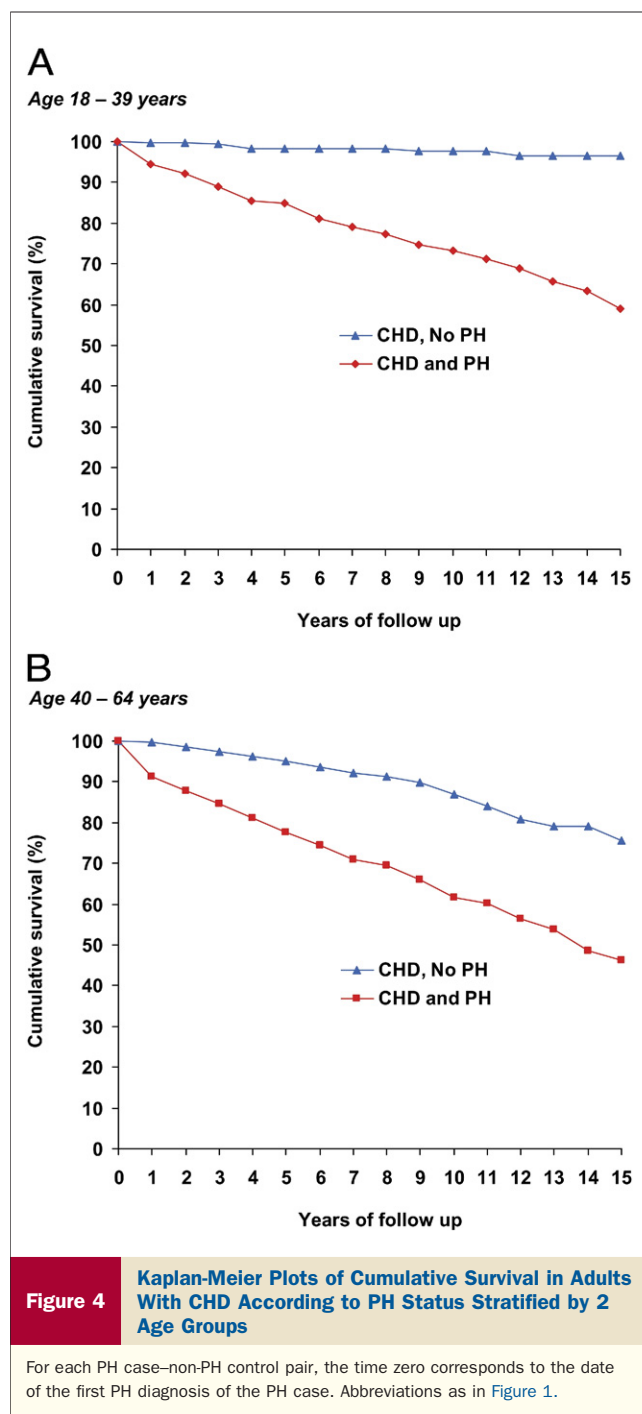
Figure 3 RRs for HSU in Adults With CHD With and Without PH

PH confers an increased rate of all health services utilization (HSU) outcomes. The rate ratios (RRs) for echocardiography and cardiac catheterization exclude those performed within 1 year of receiving the first PH diagnosis. Abbreviations as in [Figure 1](#).

more representative of the general adult CHD population. Unrestrictive ventricular septal defects (VSDs) expose the pulmonary circulation to higher pressures and are more likely to induce early and more severe pulmonary vascular disease than atrial septal defects (ASDs). However, the prevalence of ASDs in adults with CHD-related PH was higher than that of VSDs in our study. The older age of patients with ASDs and PH compared with those with VSDs and PH (median age 67.4 ± 16.9 years vs. 53.5 ± 21.4 years) is a likely explanation. Additionally, a large number of adults with restrictive VSDs, which are known to be the second most common congenital heart defect after bicuspid aortic valves (18) are included in the population-based database.

Mortality associated with PH and CHD. Published survival data of patients with CHD-related PH have been mostly limited to primary PH, selected CHD diagnoses, and Eisenmenger syndrome. Recently, mortality among adults with CHD in the Dutch Congenital Corvicia registry was compared with that among the general population (19). Pulmonary arterial hypertension predicted a 3-fold increase in all-cause mortality after adjustment for age, sex, and CHD severity. Our study reinforces the high mortality

risk associated with PH even when compared with a control population of patients with CHD without PH. The Euro Heart Survey followed 531 adults with pulmonary arterial hypertension and either ASDs or VSDs for 5 years and reported a median mortality in patients with Eisenmenger syndrome of 20.6% (10). Estimated survival for patients with PH but not Eisenmenger syndrome ranged from 93.1% with a closed VSD to 97.2% with an open ASD. In another study of patients with Eisenmenger syndrome (mean age at last follow-up 33 years), followed for a mean duration of 31 years, 35% of patients had died (4). Differences in study populations and the lack of a specific ICD-9 code to identify patients with Eisenmenger syndrome preclude direct comparisons with our study. Nonetheless, given that our population-based study likely included a greater proportion of milder CHD, the mortality risk is at least doubled with PH. We appropriately report all-cause mortality, because patients with severe PH may die of sudden cardiac death, heart failure, hemoptysis, brain abscess, thromboembolism, complications of pregnancy or noncardiac surgery (9,20,21). In a sensitivity analysis that included only patients eligible for biventricular repair, the effect of a



diagnosis of PH on mortality remained unchanged (HR: 2.69; 95% CI: 2.41 to 2.99, data not shown).

Morbidity. Morbid events have not been previously reported in patients with CHD-related PH less severe than Eisenmenger syndrome.

In the Second Natural History Study of CHD, at least 1 of the following morbid complications occurred at a rate of 123 per 10,000 patient-years of follow-up in patients with medically and surgically managed VSDs: endocarditis, heart failure, brain abscess, syncope, angina, myocardial infarction, stroke, and pacemaker implantation (6). Morbidity

related to PH was not examined in this study. Not unexpectedly, the rate of echocardiography and cardiac catheterization was significantly higher in patients with CHD-related PH than in those without PH.

Although morbidity was reported in the Euro Heart Survey, it was described in patients with cyanotic defects, with more than half having Eisenmenger syndrome (22). The reported 1.86 outpatient visits per patient-year and 71 echocardiographic evaluations per 100 patient-years for patients with cyanotic defects underscores the substantial demand on health care resources compared with noncyanotic defects.

Sex differences. In the National Institutes of Health Registry, women are affected by idiopathic pulmonary arterial hypertension, independent of age, more frequently (female/male ratio 1.7:1) (23). A Dutch nationwide registry study of adults with selective CHD reported a 25% higher risk in women (24), a result confirmed in our study. The results of our Poisson modeling an interaction term between sex and PH suggest that the differences in the sex distribution of CHD lesions most likely explains the increased prevalence of PH in women with CHD rather than biological or genetic susceptibility. This is consistent with a female predominance in CHD lesions, such as septal defects and patent ductus arteriosus, which provide an anatomical substrate for developing PH. Sex findings were remarkable for the minimal impact of sex on morbidity and mortality: when we tested the interaction between PH and sex, the impact of PH on mortality and morbidity was similar (Fig. 2) in both sexes. Our findings are consistent with those of Verheugt et al. (24), in which women had a higher risk for PH than men, but the same risk for death.

Limitations and strengths of the study design. We emphasize several limitations of our study. Foremost are misclassification errors related to PH status inherent to using ICD-9 codes as billing codes. Clinical studies have defined PH by echocardiography or cardiac catheterization (25). In our study, the quantitative results of echocardiography or cardiac catheterization were unavailable, so we describe the impact related to a diagnosis of PH by administrative coding rather than PH itself. We recognize that administrative coding reflects neither the biological onset of PH nor the severity of pulmonary vascular hemodynamic changes, and pulmonary arterial hypertension could not be distinguished from pulmonary venous hypertension. Additional clinical information for post hoc analysis was limited by the local ethics board and the Quebec government agency that approved the study, who did not allow individual patients to be identified by name or hospital number. However, the fact that our findings were applicable to all forms of PH underscores the negative prognostic implications of a PH diagnosis. Further studies are needed to differentiate the relative impact of pulmonary arterial hypertension with expected resistance changes in the pulmonary vascular bed in contrast to pulmonary venous hypertension. To address possible errors in the measurement of PH in the administrative databases, we undertook a sensitivity analysis restricted to patients with PH who

underwent cardiac catheterization within 1 year of the first PH diagnosis coding. The validity of a diagnosis of PH was supported by the high proportion of patients who underwent echocardiography or cardiac catheterization within 1 year of the first PH coding (31% of patients underwent both, and 89% underwent at least 1, of the 2 diagnostic procedures). The results of the sensitivity analysis support the validity of the main analyses, without overestimation of the outcomes with a more inclusive definition of PH. We minimized false-positive cases of PH by including coding only by selected physicians familiar with PH patients. Stricter criteria were unnecessary, because results remained unchanged in further sensitivity analyses that excluded 108 PH and non-PH pairs whose diagnoses were not made during hospitalization by cardiologists or pulmonologists (mortality HR: 2.70; 95% CI: 2.42 to 3.01). Although undercoding of PH is possible, our reported prevalence of 6% is consistent with results from another population-based study of CHD-related PH (17). False-negative cases were unlikely in the prevalence cohort, because subjects had 23 years to be identified with PH. In the matched cohort, the number of false-negative cases (subjects with PH analyzed as controls) may have been higher, but this selection bias is likely to result in more conservative estimates (assuming that the effect of PH on outcomes is never protective).

We minimized the misclassification of CHD diagnoses by using all available data for a given subject over the 23 years of database follow-up and manual audits for the CHD diagnoses on random samples of 28% of subjects (1).

Our list of potential confounders is comprehensive, but we cannot exclude residual confounding factors that are unknown or could not be measured within administrative databases. For example, the effects of cardiac surgery on PH could not be assessed, because of the limited time window of our administrative databases. However, assuming that surgery for CHD prevents the onset and adverse sequelae of PH, this unmeasured confounding factor is likely to bias the estimates toward the null.

We may have excluded subjects who failed to come into contact with the Quebec health care system during the study period. However, this is unlikely given that the study period spanned more than 23 years. Furthermore, in our previous work assessing the prevalence of CHD, on the basis of an estimated annual net migration into the province of 24,000 people, we may have overestimated the number of patients with CHD by only 0.05% (1).

Our results can be generalized to wider Canada, because Quebec accounts for one-quarter of Canada's adult population. Although this is not a U.S.-based population study, standards of care for patients with CHD have largely followed North American standards (26).

Conclusions

CHD-related PH is not rare and is associated with more than doubling of all-cause mortality and more than tripling

of morbid complications and hospitalization days compared with patients without PH. With an increasing population of adults surviving with CHD, the burden of disease associated with PH is expected to increase. Patients with CHD have been under-represented in trials of PH, and the findings of this study calls for more investigations of PH-targeted therapy in CHD. Our findings should be of interest to future health care resource planners.

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Key Words: congenital heart defect ■ morbidity ■ mortality ■ population ■ pulmonary hypertension.

APPENDIX

For ICD-9 codes for CHD, PH, and morbid outcomes, please see the online version of this article.